AMENDMENTS TO THE CLAIMS

Claims 1-68: **(Canceled)**

69. **(Previously Presented)** A method for *in vivo* down-regulation of interleukin 5 (IL5) activity in an animal, including a human being, the method comprising effecting presentation to the animal's immune system of an immunogenically effective amount of

- at least one IL5 polypeptide autologous in the animal or a subsequence thereof which has been formulated so that immunization of the animal with the autologous IL5 polypeptide or subsequence thereof induces production by the animal of antibodies against the IL5 polypeptide, and/or
- at least one IL5 analogue wherein is introduced at least one modification in the amino acid sequence of the animal's autologous IL5 polypeptide which has as a result that immunization of the animal with the analogue induces production of antibodies in the animal against the animal's autologous IL5 polypeptide.

70. **(Previously Presented)** The method according to claim 69, wherein is presented an IL5 analogue with at least one modification of the IL5 amino acid sequence.

71. **(Previously Presented)** The method according to claim 70, wherein the modification has as a result that a substantial fraction of IL5 B-cell epitopes are preserved and that

- at least one foreign T helper lymphocyte epitope (T_H epitope) is introduced, and/or
- at least one first moiety is introduced which effects targeting of the modified molecule to an antigen presenting cell (APC) or a B-lymphocyte, and/or
  - at least one second moiety is introduced which stimulates the immune system, and/or
- at least one third moiety is introduced which optimizes presentation of the modified IL5 polypeptide to the immune system.

72. **(Previously Presented)** The method according to claim 71, wherein the modification includes introduction as side groups, by covalent or non-covalent binding to suitable chemical

groups in IL5 or a subsequence thereof, of the foreign T_H epitope and/or of the first and/or of the second and/or of the third moiety.

73. **(Previously Presented)** The method according to claim 71, wherein the modification includes amino acid substitution and/or deletion and/or insertion and/or addition.

74. **(Previously Presented)** The method according to claim 73, wherein the modification results in the provision of a fusion polypeptide.

75. **(Previously Presented)** The method according to claim 73, wherein introduction of the amino acid substitution and/or deletion and/or insertion and/or addition results in a substantial preservation of the overall tertiary structure of IL5.

76. **(Previously Presented)** The method according to claim 70, wherein the modification includes duplication of at least one IL5 B-cell epitope and/or introduction of a hapten.

77. **(Previously Presented)** The method according to claim 71, wherein the foreign T-cell epitope is immunodominant in the animal.

78. **(Previously Presented)** The method according to claim 71, wherein the foreign T-cell epitope is promiscuous.

79. **(Previously Presented)** The method according to claim 78, wherein the at least one foreign T-cell epitope is selected from a natural promiscuous T-cell epitope and an artificial MHC-II binding peptide sequence.

80. **(Previously Presented)** The method according to claim 79, wherein the natural T-cell epitope is selected from a Tetanus toxoid epitope such as P2 or P30, a diphtheria toxoid epitope, an influenza virus hemagluttinin epitope, and a *P. falciparum* CS epitope.

81. **(Previously Presented)** The method according to claim 71, wherein the first moiety is a substantially specific binding partner for a B-lymphocyte specific surface antigen or for an APC specific surface antigen, such as a hapten or a carbohydrate for which there is a receptor on the B-lymphocyte or the APC.

82. **(Previously Presented)** The method according to claim 71, wherein the second moiety is selected from a cytokine, a hormone, and a heat-shock protein.

83. **(Previously Presented)** The method according to claim 74, wherein the cytokine is selected from, or is an effective part of, interferon γ (IFN-γ), Flt3L, interleukin 1 (IL-1), interleukin 2 (IL-2), interleukin 4 (IL-4), interleukin 6 (IL-6), interleukin 12 (IL-12), interleukin 13 (IL-13), interleukin 15 (IL-15), and granulocyte-macrophage colony stimulating factor (GM-CSF), and the heat-shock protein is selected from, or is an effective part of any of, HSP70, HSP90, HSC70, GRP94, and calreticulin (CRT).

84. **(Previously Presented)** The method according to claim 71, wherein the third moiety is of lipid nature, such as a palmitoyl group, a myristyl group, a farnesyl group, a geranyl-geranyl group, a GPI-anchor, and an N-acyl diglyceride group.

85. **(Previously Presented)** The method according to claim 69, wherein the IL5 polypeptide has been modified in at least one of loops 1-3 or in the amino acid residues C-terminal to helix D, said loops and said helix D corresponding to those shown in Fig. 3 for human and murine IL5.

86. **(Previously Presented)** The method according to claim 85, wherein the IL5 polypeptide is a human IL5 polypeptide.

87. **(Previously Presented)** The method according to claim 86, wherein the human IL5 polypeptide has been modified by substituting at least one amino acid sequence in SEQ ID NO: 1 with at least one amino acid sequence of equal or different length thereby giving rise to a foreign T_H epitope, wherein substituted amino acid residues are selected from the group consisting of

residues 87-90, residues 88-91, residues 32-43, residues 33-43, residues 59-64, residues 86-91, and residues 110-113.

88. **(Previously Presented)** The method according to claim 69, wherein presentation to the immune system is effected by having at least two copies of the IL5 polypeptide, the subsequence thereof or the modified IL5 polypeptide covalently of non-covalently linked to a carrier molecule capable of effecting presentation of multiple copies of antigenic determinants.

89. **(Previously Presented)** The method according to claim 69, wherein the IL5 polypeptide, the subsequence thereof, or the modified IL5 polypeptide has been formulated with an adjuvant which facilitates breaking of autotolerance to autoantigens.

90. **(Previously Presented)** The method according to claim 89, wherein the adjuvant is selected from the group consisting of an immune targeting adjuvant; an immune modulating adjuvant such as a toxin, a cytokine and a mycobacterial derivative; an oil formulation; a polymer; a micelle forming adjuvant; a saponin; an immunostimulating complex matrix (an ISCOM matrix); a particle; DDA; aluminium adjuvants; DNA adjuvants; γ-inulin; and an encapsulating adjuvant.

91. **(Previously Presented)** The method according to claim 69, wherein an effective amount of the IL5 polypeptide or the IL5 analogue is administered to the animal via a route selected from the parenteral route such as the intradermal, the subdermal, the intracutaneous, the subcutaneous, and the intramuscular routes; the peritoneal route; the oral route; the buccal route; the sublinqual route; the epidural route; the spinal route; the anal route; and the intracranial route.

92. **(Previously Presented)** The method according to claim 91, wherein the effective amount is between 0.5 μg and 2,000 μg of the IL5 polypeptide, the subsequence thereof or the analogue thereof.

93. **(Previously Presented)**The method according to claim 91, which includes at least one administration of the IL5 polypeptide or analogue per year, such as at least 2, at least 3, at least 4, at least 6, and at least 12 administrations per year.

94. **(Previously Presented)**The method according to claim 91, wherein the IL5 polypeptide or analogue is contained in a virtual lymph node (VLN) device.

95. **(Previously Presented)** The method according to claim 69, wherein presentation of modified IL5 to the immune system is effected by introducing nucleic acid(s) encoding the modified IL5 into the animal's cells and thereby obtaining *in vivo* expression by the cells of the nucleic acid(s) introduced.

96. **(Previously Presented)** The method according to claim 95, wherein the nucleic acid(s) introduced is/are selected from naked DNA, DNA formulated with charged or uncharged lipids, DNA formulated in liposomes, DNA included in a viral vector, DNA formulated with a transfection-facilitating protein or polypeptide, DNA formulated with a targeting protein or polypeptide, DNA formulated with Calcium precipitating agents, DNA coupled to an inert carrier molecule, DNA encapsulated in chitin or chitosan, and DNA formulated with an adjuvant.

97. **(Previously Presented)** The method according to claim 95, wherein the nucleic acids are administered intraarterially, intraveneously, or by the routes defined in claim 91.

98. **(Previously Presented)** The method according to claim 96, wherein the nucleic acid(s) is/are contained in a VLN device.

99. **(Previously Presented)** The method according to claim 96, which includes at least one administration of the nucleic acids per year, such as at least 2, at least 3, at least 4, at least 6, and at least 12 administrations per year.

100. **(Previously Presented)** A method for treating and/or preventing and/or ameliorating asthma or other chronic allergic conditions characterized by eosinophilia, the method comprising down-regulating IL5 activity according to the method according to claim 69 to such an extent that the number of eosinophil cells, either systemically or locally at the disease focus, is significantly reduced, such as a reduction of at least 20%.

101. **(Previously Presented)** An IL5 analogue which is derived from an animal IL5 polypeptide wherein is introduced a modification which has as a result that immunization of the animal with the analogue induces production of antibodies against the IL5 polypeptide, and wherein the modification involves amino acid substitution and/or insertion and/or deletion to any one of loops 1-3 or C-terminally to helix D in IL5.

102. **(Previously Presented)** An IL5 analogue according to claim 101, wherein the modification has as a result that a substantial fraction of IL5 B-cell epitopes are preserved and that

- at least one foreign T helper lymphocyte epitope (T_H epitope) is introduced, and/or
- at least one first moiety is introduced which effects targeting of the modified molecule to an antigen presenting cell (APC) or a B-lymphocyte, and/or
- at least one second moiety is introduced which stimulates the immune system, and/or
- at least one third moiety is introduced which optimizes presentation of the modified IL5 polypeptide to the immune system.

103. **(Previously Presented)** An immunogenic composition comprising an immunogenically effective amount of an IL5 polypeptide autologous in an animal, said IL5 polypeptide being formulated together with an immunologically acceptable adjuvant so as to break the animal's autotolerance towards the IL5 polypeptide, the composition further comprising a pharmaceutically and immunologically acceptable carrier and/or vehicle.

104. **(Previously Presented)** An immunogenic composition comprising an immunogenically effective amount of an IL5 analogue according to claim 101, the composition further comprising a pharmaceutically and immunologically acceptable carrier and/or vehicle and optionally an adjuvant.

105. **(Previously Presented)** An immunogenic composition according to claim 103, wherein the adjuvant is selected from the group consisting of an immune targeting adjuvant; an immune modulating adjuvant such as a toxin, a cytokine and a mycobacterial derivative; an oil formulation; a polymer; a micelle forming adjuvant; a saponin; an immunostimulating complex

matrix (an ISCOM matrix); a particle; DDA; aluminium adjuvants; DNA adjuvants; γ-inulin; and an encapsulating adjuvant.

106. **(Previously Presented)** A nucleic acid fragment which encodes an IL5 analogue according to claim 101.

107. **(Previously Presented)** A vector carrying the nucleic acid fragment according to claim 106.

108. **(Previously Presented)** The vector according to claim 107 which is capable of autonomous replication.

109. **(Previously Presented)** The vector according to claim 107 which is selected from the group consisting of a plasmid, a phage, a cosmid, a mini-chromosome, and a virus.

110. **(Previously Presented)** The vector according to claim 107, comprising, in the 5'→3' direction and in operable linkage, a promoter for driving expression of a nucleic acid fragment which encodes an IL5 analogue derived from an animal IL5 polypeptide wherein is introduced a modification which has as a result that immunization of the animal with the analogue induces production of antibodies against the IL5 polypeptide, and wherein the modification involves amino acid substitution and/or insertion and/or deletion to any one of loops 1-3 or C-terminally to helix D in IL5, optionally a nucleic acid sequence encoding a leader peptide enabling secretion of or integration into the membrane of the polypeptide fragment, said nucleic acid fragment, and optionally a terminator.

111. **(Previously Presented)** The vector according to claim 107 which, when introduced into a host cell, is integrated in the host cell genome.

112. **(Previously Presented)** The vector according to claim 107 which, when introduced into a host cell, is not capable of being integrated in the host cell genome.

113. **(Previously Presented)** The vector according to claim 107, wherein the promoter drives expression in a eukaryotic cell and/or in a prokaryotic cell.

114. **(Previously Presented)** A transformed cell carrying the vector according to claim 107.

115. **(Previously Presented)** The transformed cell according to claim 114 which is capable of replicating said nucleic acid fragment.

116. **(Previously Presented)** The transformed cell according to claim 115, which is a microorganism selected from a bacterium, a yeast, a protozoan, or a cell derived from a multicellular organism selected from a fungus, an insect cell such as an S_2 or an SF cell, a plant cell, and a mammalian cell.

117. **(Previously Presented)** The transformed cell according to claim 116 which is a bacterium of the genus *Escherichia*, *Bacillus*, *Salmonella*, or *Mycobacterium*.

118. **(Previously Presented)** The transformed cell according to claim 120, which is selected from the group consisting of an *E. coli* cell, and a non-pathogenic *Mycobacterium* cell such as *M. bovis* BCG.

119. **(Previously Presented)** The transformed cell according to claim 114, which expresses said nucleic acid fragment.

120. **(Previously Presented)** The transformed cell according to claim 123, which secretes or carries on its surface, an IL5 analogue derived from an animal IL5 polypeptide wherein is introduced a modification which has as a result that immunization of the animal with the analogue induces production of antibodies against the IL5 polypeptide, and wherein the modification involves amino acid substitution and/or insertion and/or deletion to any one of loops 1-3 or C-terminally to helix D in IL5.

121. **(Previously Presented)** The method according to claim 69, wherein presentation to the immune system is effected by administering a non-pathogenic microorganism or virus which is carrying a nucleic acid fragment which encodes and expresses the IL5 polypeptide or analogue.

122. **(Previously Presented)** The method according to claim 121, wherein the virus is a non-virulent pox virus such as a vaccinia virus.

123. **(Previously Presented)** The method according to claim 122, wherein the microorganism is a bacterium.

124. **(Previously Presented)** The method according to claim 121, wherein the non-pathogenic microorganism or virus is administered one single time to the animal.

125. **(Previously Presented)** A composition for inducing production of antibodies against IL5, the composition comprising

- a nucleic acid fragment which encodes an IL5 analogue derived from an animal IL5 polypeptide wherein is introduced a modification which has as a result that immunization of the animal with the analogue induces production of antibodies against the IL5 polypeptide, and wherein the modification involves amino acid substitution and/or insertion and/or deletion to any one of loops 1-3 or C-terminally to helix D in IL5 or a vector carrying said nucleic acid fragment, and
- a pharmaceutically and immunologically acceptable carrier and/or vehicle and/or adjuvant.

126. **(Previously Presented)** The composition according to claim 125, wherein the nucleic acid fragment is selected from naked DNA, DNA formulated with charged or uncharged lipids, DNA formulated in liposomes, DNA included in a viral vector, DNA formulated with a transfection-facilitating protein or polypeptide, DNA formulated with a targeting protein or polypeptide, DNA formulated with Calcium precipitating agents, DNA coupled to an inert carrier molecule, DNA encapsulated in chitin or chitosan, and DNA formulated with an adjuvant.

127. **(Previously Presented)** A stable cell line which carries a vector carrying a nucleic acid fragment encoding an IL5 analogue derived from an animal IL5 polypeptide wherein is introduced a modification which has as a result that immunization of the animal with the analogue induces production of antibodies against the IL5 polypeptide, and wherein the modification involves amino acid substitution and/or insertion and/or deletion to any one of loops 1-3 or C-terminally to helix D in IL5, and which expresses said nucleic acid fragment, and which optionally secretes or carries said IL5 analogue on its surface.

128. **(Previously Presented)** A method for the preparation of the cell according to claim 114, the method comprising transforming a host cell with the nucleic acid fragment which encodes an IL5 analogue derived from an animal IL5 polypeptide wherein is introduced a modification which has as a result that immunization of the animal with the analogue induces production of antibodies against the IL5 polypeptide, and wherein the modification involves amino acid substitution and/or insertion and/or deletion to any one of loops 1-3 or C-terminally to helix D in IL5 or with a vector carrying said nucleic acid fragment.

129. **(Previously Presented)** A method for the identification of a modified IL5 polypeptide which is capable of inducing antibodies against unmodified IL5 in an animal species where the unmodified IL5 polypeptide is a self-protein, the method comprising

- preparing, by means of peptide synthesis or genetic engineering techniques, a set of mutually distinct modified IL5 polypeptides wherein amino acids have been added to, inserted in, deleted from, or substituted into the amino acid sequence of an IL5 polypeptide of the animal species thereby giving rise to amino acid sequences in the set which comprise T-cell epitopes which are foreign to the animal species, or preparing a set of nucleic acid fragments encoding the set of mutually distinct modified IL5 polypeptides,
- testing members of the set for their ability to induce production of antibodies by the animal species against the unmodified IL5, and
- identifying and optionally isolating the member(s) of the set which significantly induces antibody production against unmodified IL5 in the animal species, or identifying and

optionally isolating the polypeptide expression products encoded by members of the set of nucleic acid fragments which significantly induces antibody production against unmodified IL5 in the animal species.

130. **(Previously Presented)** A method for the preparation of an immunogenic composition comprising at least one modified IL5 polypeptide which is capable of inducing antibodies against unmodified IL5 in an animal species where the unmodified IL5 polypeptide is a self-protein, the method comprising

- preparing, by means of peptide synthesis or genetic engineering techniques, a set of mutually distinct modified IL5 polypeptides wherein amino acids have been added to, inserted in, deleted from, or substituted into the amino acid sequence of an IL5 polypeptide of the animal species thereby giving rise to amino acid sequences in the set comprising T-cell epitopes which are foreign to the animal,
- testing members of the set for their ability to induce production of antibodies by the animal species against the unmodified IL5, and
- admixing the member(s) of the set which significantly induces production of antibodies in the animal species which are reactive with IL5 with a pharmaceutically and immunologically acceptable carrier and/or vehicle, optionally in combination with at least one pharmaceutically and immunologically acceptable adjuvant.

131. **(Previously Presented)** The method according to claim 129, wherein preparation of the members of the set comprises preparation of mutually distinct nucleic acid sequences, each sequence being a nucleic acid sequence according to claim 106, insertion of the nucleic acid sequences into appropriate expression vectors, transformation of suitable host cells with the vectors, and expression of the nucleic acid sequences, optionally followed by isolation of the expression products.

132. **(Previously Presented)** The method according to claim 131, wherein the preparation of the nucleic acid sequences and/or the vectors is achieved by the aid of a molecular amplification technique such as PCR, or by the aid of nucleic acid synthesis.

133. **(NEW)** A method of *in vivo* down-regulation of interleukin 5 (IL5) activity in an animal, including a human being, the method comprising presenting an immunologically effective amount of

- at least one IL-5 analogue wherein at least one foreign T_H eptitope is introduced into the amino acid sequence of the animal's autologous IL-5 polypeptide, whereby immunization of the animal with the IL-5 analogue produces antibodies against the animal's autologous IL-5 polypeptide.

134. **(NEW)** The method according to claim 70, wherein the modification preserves a substantial fraction of IL5 B-cell epitopes and that at least one natural promiscuous T-cell epitope is introduced.

135. **(NEW)** The method according to claim 70, wherein the modification preserves a substantial fraction of IL5 B-cell epitopes and that at least one APC specific antigen is introduced.

136. **(NEW)** The method according to claim 70, wherein the modification preserves a substantial fraction of IL5 B-cell epitopes and that at lease one palmitoyl group is introduced.

137. **(NEW)** The method according to claim 70, wherein the modification preserves a substantial fraction of IL5 B-cell epitopes and that at least one cytokine is introduced.

138. **(NEW)** The method according to claim 79, wherein the natural T-cell epitope is a tetanus toxoid epitope.

139. **(NEW)** The method according to claim 78, wherein the at least one foreign T-cell epitope is a natural promiscuous T-cell epitope.

140. **(NEW)** The method according to claim 74, wherein the cytokine is granulocyte-macrophage colony stimulating factor (CM-CSF).

141. **(NEW)** The method according to claim 74, wherein the heat shock protein is calreticulin (CRT).